

REMARKS

The above amendments cancel claims 1-38 and add new claims 39-45 to the application. Reconsideration of the rejections made in the office action dated November 16, 2004 is respectfully requested in view of the above amendments and the following remarks.

The new claims are supported by the originally filed claims as well as page 2, lines 19-22. One example of a substance that acts on a growth factor precursor is CRM197, a catalytically inactive form of the diphtheria toxin which specifically binds to pro-HB-EGF and is discussed on page 3, lines 15-16 of the present application.

The previous claims were rejected under 35 USC §102(a) over Dong et al. The present claims include a step of "contacting the cell with a compound which acts on a growth factor precursor in a G protein mediated extracellular signal transduction pathway". Dong does not disclose such a step as Dong suggests only Batimastat, which is a compound which acts on a metalloproteinase. In addition, applicants respectfully point out that the addition of EGF as disclosed in Dong, does not activate the G-protein or GPCR initiated extracellular signal transduction pathway. The addition of EGF causes a stimulation of EGFR which is different from the stimulation which proceeds via the G-protein or GPCR initiated extracellular signal transduction pathway as required in the present claims. Figure 4 in the present application shows the influence of the addition of various reagents such as TPA, bombesin, carbachol and EGF, on the stimulation of the GPCR-initiated signal transduction pathway. This stimulation is shown by

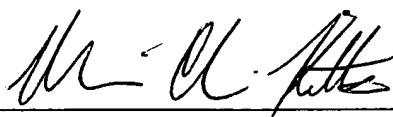
the detection of processed HB-EGF-1 (Fig 4A). Though the detection of processed HB-EGF-1 is possible after the addition of TPA, bombesin, and carbachol, no HB-EGF-1 is detectable after preincubation with EGF (fig. 4a, right column). Figure 4a in the present application clearly shows that EGF, in contrast to TPA, bombesin and carbachol, is not an activator of the GPCR initiated signal transduction pathway. In view of this, applicants contend that Dong does not show stimulation of the G-protein of a GPCR-initiated extracellular signal transduction pathway or contacting the cell with a compound which acts on a growth factor precursor as required in the present claims.

Applicants respectfully submit that claims 39-45 are now in condition for allowance. If it is believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

By



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